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# THE RÔLE OF BACTERIA IN INFECTIOUS DISEASES.

By HENRY O. MARCY, A.M., M.D.,

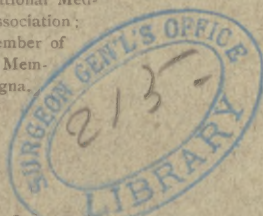
BOSTON, U. S. A.,

President of the Boston Gynæcological Society; late President of the American Academy of Medicine; Member of the International Medical Congress; Member of the British Medical Association; Member of the American Medical Association; Member of the Massachusetts Medical Society; Corresponding Member of the Medico-Chirurgical Society of Bologna, Italy; Late Surgeon U. S. A., etc.

Read before the American Academy of Medicine, Baltimore, Oct. 28, 1884.

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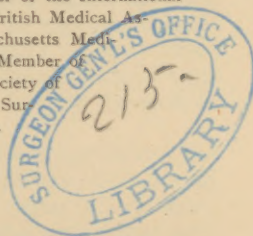
# THE ROLE OF BACTERIA IN INFECTIOUS DISEASES.

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## THE RELATION OF BACTERIA TO INFECTIOUS DISEASES.

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No subject in medicine either in relation to its theory or practice holds at present in any considerable degree an interest equal to that of the rôle of micro-organisms to disease. Although in a strict sense not new, it is only within a very recent period that systematic study and scientific research have invested the theme with an interest by any means general, or elevated it from the domain of speculative philosophy and pseudo-science. Recent as have been the investigations, it is marvellous to find the flood of literature already contributed.

Notwithstanding the interest and importance of the subject, this contribution might not have been added to the list had I not listened to a series of six semi-popular lectures delivered in Boston within the year, in which course the entire subject was carefully reviewed and in a most labored argument it was deduced that the fundamental basis is wanting upon which the entire system of the germ-theory of disease is founded; that there is no real proof that fermentation even, is caused by the development of a low order of vegetable organisms. This sweeping assertion was based upon the statement that the various classes of micro-organisms in any of the series of experiments had never been separated from the "ambient, organic, living matter" which must be considered to have a low degree of inherent vitality, and that, as a consequence, it can not be determined what, in the subsequent changes, is due to the germ

development and what the rôle of the ambient living matter may be. This, in the mind of the objector, would pertain as distinctly and definitely to the so-called pure cultures, or many removes from the primary infection, where, it is obvious, that only an infinitesimal quantity of the original material could remain, since the ambient living matter might have been reproduced indefinitely as well as the mingled germs. With an emphatic pointing of the argument it was declared "that not until it had been demonstrated, what would ensue, after a well-washed micrococcus or bacillus had been isolated upon the point of a needle and then introduced into a sterilized, nutrient solution would the real conditions of the problem be fulfilled."

Anything may be doubted. There are many who would not accept the demonstration of any historic fact; and even mathematical formulation, or axiomatic truth would by some be questioned. However, it is well to have even the old, established creeds and codes occasionally reëxamined and reviewed by the keen criticisms of opponents, for "Science is only pure and simple truth," and never suffers by test.

Negative proof may assume a value not less than positive demonstration, and yet, when we come to accept the gauntlet thus thrown down, we shall find the defenders of the germ-theory are not reduced even to this exigency. Let us separate the problem as formulated by Dr. Longstreth into its component parts, the ambient, living matter and the germ. We grant that the former has, under certain conditions, an inherent vital power, which is indeed no new discovery, but has been accepted by many of the best investigators. It has been known under different names, but, perhaps, most widely under the excellent definition given by Dr. Lionel Beale as bioplasm. In the differentiation of the organic material which serves as food,

there must evidently be somewhere along the series a point where the protoplasmic masses are imbued with a certain vital power. Let us admit that this hypothetical point be accepted as bioplastic, that the material in a considerable share is particulate, and that it has its highest expression of effect when in the greatest degree "ambient." I think we may safely assume that in the blood of a healthy animal we should find this ambient living matter in its highest potency. In order to determine the bioplastic powers of the liquid, ambient, or protoplasmic matter, I decided upon a series of careful laboratory studies, in the execution of which I am greatly indebted to my assistant, Dr. Samuel N. Nelson. The blood of healthy animals, sheep and oxen, was taken with careful precaution at the abattoir in flasks, sterilized by heat and immediately protected by carbolized gauze. As soon as the blood clot had separated by standing, sterilized glass bulbs were filled and sealed in the flame, and others charged with sterilized, culture fluids were inoculated in varying proportions, following the method which I have adopted in the study of germicides and micro-organisms. These were kept for different periods of time subject to the same conditions as in the growth and testing of various bacterial organisms. Careful microscopic examinations were made at different data with a Zeiss fourteenth objective, giving an amplification of about a thousand diameters. In only one of more than twenty bulbs did any change take place, and this upon its first opening, the third day, remained sterilized. Albumen from the egg yet warm from the nest, milk aseptically milked and put up at once, and the aqueous humor were also tested. In a series of forty-five bulbs, only two contained bacteria-termo and micrococci, which evidently were accidentally introduced, since one was a sterilized bulb inoculated with serum, and the other was fertilized when opened a second time the seventeenth day, which

was sterile upon the ninth day when first examined. In the rest of the series no changes ensued, and no micro-organisms developed. See table.

RESULTS OF TESTS WITH "AMBIENT ORGANIC MATTER."

SUBSTANCES.	TOTAL.	NO.	DAYS.	RESULTS (F. 3.)
Serum from sheep's blood.	7..	4	6	Some protoplasmic masses as in fresh serum
		I	9	ditto.
		I	11	ditto.
		I	16	ditto.
Bulbs inoculated with sheep's serum.	18..	5	6	Five unchanged, one contained micrococci and bacteria termo active.
		2	9	Unchanged protoplasmic masses.
		II	11	ditto.
		I	16	ditto.
		8	17	ditto. Also one opened at 9th day contain micrococci and bacteria termo active.
		I	8	Same protoplasmic masses this one inoculated after nine days.
Serum from ox's blood.	2	2	6	ditto.
Bulbs inoculated with ox's serum.	4	2	6	ditto.
		2	17	
Aqueous humor sheep's eye.	2	2	6	ditto.
Inoc. aqueous humor sheep's eye.	3	3	6	ditto.
Inoc. milk.	4	3	4	ditto with same.
		I	5	ditto "
Albumen of egg.	2	2	5	ditto.
Inoc. ditto.	3	3	5	ditto.
Total, .....	45			

It seems from the above experiments a clear deduction that the ambient living matter, upon the germinal qualities of which so much emphasis has been placed, possesses no power of reproduction, and that, at the most, it is an organic nutrient fluid serving the high-

est purpose for bioplastic uses, but having in itself absolutely no independent, inherent power of growth,

This, indeed, is what has been assumed *a priori* to be true by most investigators and, so far as I know, had never before been questioned. Blood serum has been selected by many of the most distinguished observers as the best possible culture fluid for the growth of micro-organisms, never suspecting that in the fluid itself there could be a source of error.

Numerous experiments familiar to all students of the subject have conclusively shown that when blood has been taken under proper precautions from a healthy animal, it undergoes no decomposition and is absolutely free from all bacterial organisms. The only objection to blood as a culture medium has been found in the presence of the corpuscles, which, after a time, may break up and present a granular debris, thus rendering the recognition of micrococci more difficult.

This is not the occasion to enter upon the character or the classification of micro-organisms. At the present, no one denies their vegetable nature. That they are organic and have an inherent, independent vitality is proven by their distinctive shape elements, spontaneous, independent movement and powers of reproduction. The rôle or relationship of these minute organisms to disease is a question the importance of which cannot be over-estimated, and, if the relationship of cause and effect in the class of zymotic diseases be demonstrated, medicine will at last have for its foundation a scientific basis.

Although we may accept the formulation that, "Science is pure and simple truth," no question probably ever presented, the solution of which is involved in greater difficulty. It is very doubtful if the time has arrived when generalization may be made or formulation adopted.

In the rapidly accumulating evidence from many

independent investigators, however, it is not too much to believe that such a period may belong to the early future. To demonstrate the causal relationship of germs to disease, the micro-organism in question must be isolated, or separated from any other material which could be called in question, be it "liquid ambient matter," organic, or chemical poison having relationship to the disease. This organism thus separated must, upon inoculation into the tissues of a healthy, living animal of the same species, cause a reproduction of the disease under consideration, in other words, the micro-organism must "breed true."

The objection already referred to was that, to carry out the requirements here given, "the germ must be isolated, well washed, and then introduced into a sterilized, culture fluid."

To accomplish a purpose, believed to be equally satisfactory, the process of so-called pure culture has been devised. This is to infect a sterilized bulb or solid culture with a minute quantity of the original virus, and upon development to inoculate from this a second, and so on to the end of a given series. Pasteur was among the first to devise this method, and show the extreme subdivision of the original material thus obtained. I quote an illustration of this from the experiments of Dr. Sternberg: "My culture-tubes contain about a fluidrachm of sterilized bouillon. The amount of infective material introduced into culture No. 1, as seed, was considerably less than a minim; but for convenience I will suppose that one minim is used each time to start a new culture; that is, the original material is diluted 60 times in the first culture, 3,600 times in the second, 216,000 times in the third, and in the eighth culture it will be present in the proportion of 1 part in 1,679,611,600,000,000. Yet a few minims of this eighth culture possesses all the virulence of the first."

Let us grant that a certain quantity of the so-called

sepsin, a chemical poison of any conceivable virulence, accompanied the primary infection, and that it was possible for it to be produced by chemical changes set up in the nutrient fluid *pari passu* with the growth of the organism; then we would find that upon subcutaneous injection into an animal it would act promptly and bear an effect in direct relation to the quantity thus used, either killing the animal, or being eliminated and recovery ensue. Contrast the effect of a septic inoculation. Hours after the injection the animal appears in its usual health, and slowly sickens. If death ensues, it is never until sufficient time has elapsed to allow the reproduction and growth of the micro-organisms; and, upon examination, the tissues and fluids are found to contain, in active development, immense numbers of organisms, in morphological characteristics identical with those of the original infection. These experiments may and have been repeated in long series with unvarying result. In still further evidence that the morbid poison is particulate and dependent upon the micro-organisms present, the experiment of filtration has been repeatedly made where the most virulent of septic, poisonous material was thus treated, and the filtrate injected into a healthy animal with negative results. Klebs first showed that filtration caused anthrax blood to lose its infectious properties, although the filtrate acted as a local poison. Toussaint repeated these experiments with similar results, and Eberth's experience with the filtrate of diphtheritic poison gave at the points of injection only local inflammations, without any marked general symptoms.

In anthrax, where the rôle of the bacilli has been very carefully demonstrated, seemingly beyond the denial of the most captious critic, only recently did I hear it publicly and seriously urged that death was not caused by the bacilli of anthrax, but was mechanical, and, as it were, accidental, since the extraordin-

ary size of the bacilli caused a plugging of the capillary circulation in the lung, and death ensued as by strangulation.

How such puerile objections could for a moment be seriously advocated, or accepted, acknowledging but ignoring the *causa causans* of disease, is beyond comprehension. However, by such queries, we are led to consider, if disease and death are the result of the growth and development of such organisms in the living body, in what way is such result brought about? Is it by occluding the blood-vessels, causing stasis, arrest of circulation, and, as a result, local death of tissue; *i. e.*, mechanical? Does it devitalize the tissues by abstraction of nutriment for its own uses, deoxydizing the blood? Does it also generate in its growing a morbid virus which is inimical to life; or does it, by its abstraction of certain constituents necessary to its development, cause chemical changes in the construction of highly organized, vital elements, as the yeast plant in its growth in saccharine solutions produces alcohol?

There can be little doubt but that in each of these several ways, sometimes separately, more often combined, does injury result by the development of these minute organisms. Did it not carry us beyond our present limits we should discuss the individualistic resistance to the invasion and growth of micro-organisms within the body of the living animal. This must, at least in a large share, be ascribed to a property in the living organism, a vitality which renders the development of the bacterial growths abortive, or imperfect. Reduce this standard, lower it to a hypothetical given point, and the complex organism becomes an easy prey to the omnipresent, unseen, yet potential forces which are ever in waiting to take it to pieces and refit it for new and perhaps higher uses.

The vital equations in the life processes are among

the most complex and difficult of all in the study of the animal economy. They meet us at every turn when we investigate any of the pathological changes. The reason why, in some animals, micro-organisms cannot be made to grow at all, while in others, seemingly equally healthy, they fructify and speedily cause death, must be sought in the peculiar vital or resisting power of the individual or the species. This has evidently been overlooked or underestimated by many in their deductions upon this subject. The cell changes which follow localized irritation furnish an excellent illustration. Lymphoid, epithelioid cells, or granulation tissue, is proliferated in protection and, in the development series, connective tissue ensues and repair is completed. Arrest the process at its earlier stages and degenerative changes take place, and it is in this way that conditions are produced favorable to germ development. Thus, simple depreciation of vital force may be the first term of a series ending in death, to which, as it were, are added only accidental factors.

There are many questions relating to the subject upon which we are at present and perhaps must ever remain ignorant. How do certain forms of infectious disease grant immunity from subsequent attack? Answers only of a purely speculative character have as yet been suggested. In what way, upon recovery from attack, do the morbid, germinal materials disappear? Here again all positive demonstration is wanting. Sternberg suggests that the disappearance of the bacteria from the circulation may be effected by the superior vitality of the white corpuscles which in their amoeboid motions may surround and assimilate the captured bacteria.

What are harmless and what are pathogenic bacteria? May the one develop from the other; are they modified by the media in which they grow, may a micrococcus develop into a bacillus, a bacillus into a spirillum? Do each of the infectious diseases have

its *sui generis* germ? These again are questions of intense interest engaging the attention of many scientists at the present, but upon which little can be declared as settled. Reviewing these phases of the subject, beset with so many difficulties, it is encouraging to be able to differentiate somewhat clearly, however, the known from the unknown, and to be certain of the establishment of facts of fundamental value and importance.

In this review of the more recent demonstrations of the germ-theory, we must limit ourselves to a small number of diseases. The study of anthrax is the most instructive because the most complete and demonstrative. Pasteur followed a series of one hundred cultures to find the last as virulent as the first. Koch continued the experiments in septicæmia with mice to over fifty repetitions, not only to demonstrate the breeding true, but also that as a rule one-tenth of a drop was an ample quantity to induce a fatal result. Contrary to that found in anthrax, the bacilli here are extremely small.

The rôle of the bacillus tuberculosis has been so satisfactorily established by Koch that a large number of our best observers accept the conclusion of cause and effect as demonstrated. No one subdivision of the question probably holds an interest and importance equal to this at present. Dr. Fergerson publishes in the *Medical Record*, July, 1883, a compilation, as a statistical table, in which he states that in 2,509 cases reported, 2,417 cases contained bacilli. The most noteworthy fact in reference to the cultivation experiments of the bacillus tuberculosis is their slow growth. Koch cultivated them at a temperature of one hundred and four. It was not until the tenth day that active development supervened. Five successive cultures occupied fifty-four days. With this culture four guinea-pigs were inoculated, and upon the thirty-fifth day all were found undergoing exten-

sive tuberculosis. A series of injections into the eye gave somewhat similar results. One inoculated with pure serum, "liquid ambient matter," remained healthy. Three inoculated from a series of cultures which had been carried on for one hundred and thirty-two days gave reproduction of typical tuberculosis. Similar experiments with greater or less care have been repeated in various countries giving in large share confirmatory evidence. In the discussion of the subject, unfortunately the partisans of their various views have often lost a wise judicial discrimination, and at such hands the advancement of science suffers.

Dr. Formad, of Philadelphia, has imparted much knowledge in his publications upon the subject, but he has failed in his attempts to reproduce from his so-called tubercle of irritation true tuberculosis.

Evidently the first point to define is, what is tubercle? If only consisting of lymphoid, embryonal, or epithelial cell-growth, more commonly known to us as a low order in vitality of granulation tissue, then we must admit with him that any irritant may produce tubercle, and the more finely divided and widely disseminated the irritant, the more finely miliary and widely diffused the resultant tubercle.

If it can be shown that such tuberculous material, devoid of germ infection, will reproduce upon inoculation into healthy animals, resulting in disseminated tuberculosis, and so on in a given series, then the objections and negative evidence will stand upon the same basis as the positive, and we will be ready to admit the exclusive production of tubercle as not due to bacillary infection. This we had expected would be shown by Dr. Formad, since in his second report which he has published upon the subject he states: "In my own experiments, I found that tubercle produced by inoculation with innocuous material under antiseptic precautions was likewise capable of producing tubercle when inoculated into other ani-

mals, having thus the same action as the innocuous material primarily used." Dr. Formad believes the rôle of the bacillus in tuberculosis is simply that of an irritant.

Malassez and Vignal have recently published a most interesting series of studies, experiments, and observations upon tuberculosis produced by micrococci in zoöglea masses in which no bacilli were found. The following are in brief their conclusions:

1. There exist tuberculous lesions presenting no bacilli, and which inoculated give place to tuberculosis equally without bacilli, and yet similar in appearance to bacillary tuberculosis. Similar results were obtained with their culture products. If the presence of the bacillus suffices, according to Koch, to characterize the tuberculous nature of a lesion, the reciprocal is not true, namely: their absence does not suffice to deny the tuberculous nature of a lesion.

2. In tuberculosis from inoculation without bacilli there are tubercles which are characterized by the presence of zoöglea masses of micrococci which play, in the tissues which they infect, the rôle of foreign irritating bodies and determine in them thus the so-called tuberculous lesions.

3. There are also other tubercles of inoculation, not bacillary, in which we distinguish no well-defined zoöglea masses. They seem due to the presence of micrococci of the same kind as those of the zoöglea masses, but which, instead of being grouped in masses, are strewn through the tissue of granulation and it may be just this dissemination, which, in absence of the special coloring reagent, prevents distinguishing them sufficiently. That which proves this is, that they may, by inoculation, produce anew zoöglei tubercles. It may be possible that these are some in which that form of parasite may have indeed disappeared.

4. These same tubercles, not bacillary, with or with-

out distinct zoöglea, may produce after a greater or less number of generations of inoculations, bacillary tubercles, as if the zoöglea, the diffused micrococci, and the bacilli were simply different forms, or different stages of development of one and the same micro-organism. Yet this transformation from micrococci into bacilli, not having yet been directly established, we have no right to affirm that bacillary tubercle and zoöglea tubercle are of the same nature, although it may be perhaps the most probable hypothesis.

5. Although our zoöglea masses and our micrococci do not closely resemble the described parasites previously mentioned by Klebs, Aufrecht and Toussaint, they may, however, be in some way related to them; but the facts observed do not permit us to determine the question.

There is much difference of opinion upon the communicability of tuberculosis.

Dr. Formad denies that any proof has been produced showing communicability.

Dr. Dreshfield gives the following instance: "In a small town in Germany where in the period of nine years only five children had died of tubercular meningitis, there happened in the course of nine months eleven deaths from that disease in infants under six months, all these children had been assisted into the world by a midwife who was known to be phthisical and who died of phthisis and who was in the habit when attending a confinement to blow into the mouth of the child with the view of expanding the lungs. No mention is made of the number of confinements attended by this woman."

Dr. MacKenzie in the February number, 1884, of the *Edinburgh Medical Journal* details the result of examinations made in seventy cases of pulmonary and laryngeal disease. A little over one-half were well-marked cases of tuberculous disease and in all

these the bacilli were found in the sputum and most abundant in the acute cases. The muco-pus taken from the larynx in laryngeal phthisis contained bacilli in abundance. In thirty-three cases bacilli were absent, of which twenty-two were undoubtedly non-tuberculous, and the remainder, although of doubtful character at the time of examination, were proven by their subsequent examination not to be of tuberculous origin.

Bacilli have been found in glanders, intermittent fever, leprosy, malignant oedema, syphilis, and cholera with more or less evidence that they are the producing cause. Dr. Salisbury in our own country was probably the first to declare that the cause of intermittent fever was a minute vegetable growth. His experiments were numerous and made with a care worthy of commendation, when we consider that he was a pioneer in the field. That they were inferential instead of demonstrative is true, but he collated a series of facts and array of evidence which renders his observations valuable and well worthy of honorable mention.

Klebs and Tommosi-Crudeli announced the discovery of the bacillus malaria in 1879. Their experiments were made in the vicinity of Rome and have been repeated with confirmatory results by a number of Italian and German observers.

Dr. Sternberg<sup>1</sup> in New Orleans, in 1880, instituted a series of experimental studies with only negative results. He gives a critical review of the subject at some length and arrives at the conclusion that demonstrative evidence of the *sui generis* micro-organism is yet wanting. He found in the swamp mud near New Orleans and in the gutters of that city bacilli which closely resembled the described organisms. While the proof is wanting that these actually cause intermittent fever, he closes the discussion as follows:

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<sup>1</sup>Bacteria. Page 317.

“On the other hand there are many circumstances in favor of the hypothesis that the etiology of these fevers is connected, directly or indirectly, with the presence of these organisms or these germs in the air and water of malarial localities.”

There can be no doubt of the importance of a better knowledge of soil pollution and in this connection I would call attention to the admirable original work done by Profs. Pampelly and Smythe, incorporated in their report to the National Board of Health. I am informed that a large amount of original, experimental research by the same authors still awaits publication, because the appropriation therefor was withdrawn.

Last autumn, during the construction of a large sewer in Brookline, to convey the waters of Muddy Brook, used for a long time as an open sewer, the bottom of the excavation was eighteen feet below the crossing roadway. The cut was through a stiff clay marl. In a specimen of this material taken from the very bottom, were found bacilli perhaps a trifle longer, but otherwise not unlike in their morphological characteristics to the bacillus tuberculosis. They were easily reproduced in sterilized bulbs, but no inoculation experiments were attempted. Last winter I examined a specimen of the clay taken from the bottom of a sewer excavation in Beacon St., Boston, in which I found abundance of active micrococci. The cut had extended through the filling into the solid clay substrata and was probably more than twenty feet below the surface.

Dr. Andrew Smart, of Edinburgh, published a description of micro-organisms, with drawings, found in the disease called Rinderpest, in 1865. This is claimed to be the first demonstration of bacteria in living tissues.

In glanders several independent observers (Struck, Löffler, Israel, and Bouchardt) have found a bacillus

and cultivated it. When inoculated into the nasal cavity of animals (horse and rabbit), it has produced typical glanders. Hansen, of Norway, has made a most interesting series of studies upon leprosy. In the tubercles or nodules he finds a bacillus which he describes and figures. It is in appearance not unlike the bacillus tuberculosis, and Neisser has confirmed Hansen's demonstrations. The bacilli were successfully cultivated, but the inoculation experiments have given only negative results.

A simple review of the work done in the study of the relation of micro-organisms to typhoid fever would in itself make an interesting paper. When we remember the intestinal canal in health is the home of an infinite number of actively growing bacilli, we can at once appreciate one of the difficulties which meets the observer at the very outset. These, undoubtedly, infect the ulcers and necrosed tissues; but by a number of observers, notably Eberth,<sup>1</sup> bacilli have been found in the mucous membrane, lymphatic glands, and spleen. Koch is of the opinion that the bacillus of Eberth is the only one which holds to the disease a specific relation. It is a short, thick rod, and stains less deeply than the bacilli of putrefaction. The member of the bacillary family which seems to play a specialistic part in the causation of disease, latest discovered, has been reported by Dr. De Lærada, of South America, as the bacillus of beri-beri. His studies were carried on after the method of Pasteur, in the physiological laboratory of the National Museum at Rio Janeiro. Beri-beri is an obscure disease, introduced many years ago into Brazil from India, and in certain provinces is very fatal. Bacilli were found in the blood, but especially in the muscles and spinal medulla. These were isolated by cultures and inoculation experiments produced a reproduction of the disease in animals.

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<sup>1</sup> "Der Typhus-Bacillus und die intestinale Infection."

From these again cultures were made and the series reproduced. It is believed the origin of the disease is found in certain conditions incident at times to the rice, and in the districts most subject to the disease rice is the principal article of food. Micro-organisms not unlike those of beri-beri were found on the rice, were cultivated, and injections of the culture were made, using guinea-pigs; death occurred from thirteen to twenty days with paralysis, and bacilli were found in the spinal cord and muscles. The demonstration seems complete, but farther investigations are promised.

Dr. Sternberg's admirable report of the Havana Yellow Fever Commission must be briefly referred to. His studies of the blood were certainly made with the utmost care, and his photo-micrographs are of the greatest perfection and beauty. From the present better knowledge of the rôle of micro-organisms in disease, it is questionable if more satisfactory results might not have been obtained, if the lymphatic and glandular systems had been equally carefully studied. Although he demonstrated no micro-organism which could be considered as causal, there are a number of observers who claim to have found it. Dr. Freise, of Brazil, describes an organism which he thinks may remain indefinitely in the soil, and which he finds rapidly reproduced with fatal results in rabbits and guinea-pigs. His observations would, however, seem to require confirmation. The whole subject demands a most complete and painstaking examination.

Cholera holds the first place in popular interest at the present time, owing to its ravages in Europe, and the widespread fears that it may yet become far more general, and extend to America.

The medical profession have followed with an intense interest the investigations of the cholera commissioners in Egypt and India during the last year.

Their reports must be considered by all as of great importance, and are contributions of especial scientific value. Few questions can be more complex, or investigated amid such an array of difficulties. The micro-organisms which in health infest the digestive tract are various, and in numbers utterly incomprehensible. Their histories and the modifications which they undergo, subject to a great variety of diseases, are but little known. Much work by reliable observers is requisite as a preliminary to the satisfactory study of an epidemic of cholera. I would urge that the attention of all practitioners possessing the requisite knowledge, should be given to a careful study of such conditions, and thereby contribute to the solution of many questions yet unsolved.

Another difficulty, which does not pertain to the study of many pathogenic germs, is the well-established fact that cholera does not infect the lower animals. Hence the very important evidence deduced from inoculation experiments with the organisms or their cultivations is here wanting. In the sixth cholera report written by Dr. Koch, it is stated that the bacilli which, in their earlier reports, the Commission were unable to determine as strictly limited to cholera, were now accepted by them as holding a specific relationship. The distinguishing characteristics given to the organisms are, briefly: "They are not quite straight, as are the other forms of bacilli, but are slightly curved, comma-like; this bending may be even so marked as to be almost semicircular. From these curved stems, S-shaped figures, more or less elongated, slightly undulating, linear forms may be developed in pure cultivations, of which the first two segments and the last correspond to the form of the bacilli as found in cholera, and which, continually increasing in number, remain attached to one another." Thus they closely resemble a spirillum, and may ultimately be classed with

it. The voluntary movements were very active. These bacilli were found in all the intestinal discharges, and in the contents of the intestinal canal at post-mortem examinations, but not in any other disease, and only in one instance in the various specimens of dirty water examined.

Dr. Koch, in discussing the relationship of these growths, states that the development of the supposed specific bacteria can only be favored by the cholera process, or that the bacillus is the cause of the disease, and that the disease is only induced when it has found its way into the intestine of man. If the first supposition is allowed, these bacilli are always present in health, which is stated as not the fact. Therefore he concludes that the growth of the bacteria cannot be due to the cholera process, and there is nothing left but the inference that it is itself the cause of the disease. Many other circumstances are emphasized as pointing to the same conclusion. They are limited to the organ which is the seat of the disease. They invade its tissues, which become markedly metamorphosed. In the earlier dejections of a cholera patient, so long as they are still feculent, the bacilli are few, but the subsequent watery, nearly odorless, characteristic dejections contain the bacilli in immense numbers, and coincidently all other bacteria disappear almost completely, so that in this stage of the disease an almost pure cultivation of the bacilli is obtained; conversely, the comma-like bacilli decrease and disappear completely during convalescence. This general relationship holds good, also, as observed from post-mortem examinations. There can be no doubt but the study of the present epidemic will contribute much to our knowledge.

The great majority of observers in India and elsewhere give it as their unqualified opinion that cholera is infectious, and may be transmitted not only from

individual to individual, but in a variety of ways to great distances.

From this belief has arisen the very generally adopted system of quarantine. It is greatly to be deprecated that the English government, under advisement of Drs. Hunter, Foyer and Cunningham, themselves not only very distinguished men, but especial observers in Egypt and India, has given official expression to its disbelief of the value of quarantine regulations.

“Her Majesty’s government offers a serious and well-founded objection to the theory generally admitted and the custom of quarantine. Sanitary measures have proved to be the only efficacious means of impeding the march of an epidemic.”

I am free to confess, this was my own opinion formerly, and I held quarantine regulations to be respected simply because they had been formulated as laws. I must now think otherwise, since the weight of evidence would render it hard for the unprejudiced, judicial student to disbelieve in the communicability of cholera. A large volume itself would not contain the facts already collated. Dr. C. Macnamara, in a lecture published in the *British Medical Journal*, March 15, 1884, upon Asiatic cholera, states that for a long time he could not himself subscribe to the communicability of cholera, but a careful historical research convinces him of the fact, and he gives this illustration of his own personal experience: “A small quantity of a fresh rice-water stool, passed by a patient suffering from cholera, was accidentally mixed with four gallons of dirty water, and the mixture exposed to the rays of the tropical sun for twelve hours. Early the following morning nineteen people each swallowed about an ounce of the contaminated water; they only partook of it once, but within thirty-six hours five of these nineteen persons were seized with cholera. In this case the cholera evacuation did not

touch the soil ; as it was passed, so it was swallowed, but (and this is the most important part to remember) it had been largely diluted with impure water, and the mixture had been exposed to the light and heat of a tropical sun for twelve hours. In the year 1872 I was engaged in making some experiments on monkeys. For this purpose I exposed to the sun some fresh cholera dejecta in a pail full of dirty water. The following morning, at about 6:30 A. M., I and my assistant were shut up in a close room with these monkeys, experimenting upon them with this diluted cholera stuff. By 2 o'clock the same day I was suffering from a severe attack of cholera, and the same evening my assistant was seized with the disease. We were both of us very dangerously ill, passing into a state of collapse in a few hours after the commencement of the symptoms. The monkeys escaped without the slightest ill effects from our endeavor to give them cholera."

In the same journal for October, 13, 1883, (page 727) Surgeon General James Irving of the Bengal Army adduces certain facts showing the conveyance of cholera in India and they seem so conclusive that I briefly reproduce a portion of them here: Surgeon-Major H. B. Purves was stationed at Darjeeling in 1876. This is in the Himalayas, forty miles above the plains, 7,000 feet above the level of the sea and approached by a single road. The population was scanty, the climate healthy, and numerous tea gardens were scattered about the adjacent country. "Early in June, there was a regular cholera wave over the whole district, lessening in the plains, but rapidly increasing among the hills. Large gangs of coolies who had bolted from the lower ranges, had entered the hills, and were roaming about the forests, in some instances carrying their sick with them." In July a great and general improvement took place, and by August the disease had disappeared. The mortality

reported by the police (who are the collectors of medical statistics in India), was 1,729 out of a population of 94,712, though Mr. Purves considers that there were at least twice as many deaths. Mr. Purves instances "special cases where human intercourse seemed undoubtedly to be the immediate cause of the appearance of cholera." He does not name the gardens referred to, but alludes to them by numbers.

"Garden No. 1.—The disease had been prevalent for some time at an adjoining estate. No case occurred until a man happened to go to the infected garden to bury his sister, who had died of cholera. Shortly after his return, he was attacked and died; and the result was a severe and fatal outbreak, causing a mortality of 150 among a population of 1,500.

"Garden No. 2.—The manager states that the infection was distinctly traced to communication with a bazaar close by. Seven hundred deaths.

"Garden No. 3.—It was discovered that new coolies from an infected garden had lately settled in the lines when the first case occurred. Eighty-five deaths among 650.

"Garden No. 4.—The outbreak was traced beyond doubt to the advent of new coolies from infected parts of the terai. Two hundred and eight deaths in 1,700.

"Garden No. 5.—Eight new coolies offered themselves for employment at a garden near Darjeeling and were entertained. Shortly afterwards, cholera broke out among them, and every one of the eight died. It was ultimately discovered that they had fled from an infected garden in the terai. The other coolies, who had hitherto been healthy, were also infected by the new-comers.

"Garden No. 6.—Seven new coolies from an infected part of the Kursang neighborhood arrived at a hill garden on which there had been no signs of cholera. Shortly afterwards the disease broke out; and, in

twenty days of June, 72 died from the disease out of a total population of 100. It is worthy of note that a few villagers living in scattered huts in the same garden, but not working as coolies, escaped entirely."

Certain enthusiastic sanitarians, especially English, encouraged by the semi-official statements of governmental character, have lately broadly asserted that cholera cannot be communicated or transmitted, but is a local disease dependent upon pollution of the atmosphere, water, or soil. Sir W. G. Hunter, in his observations in Egypt, emphasized as cause the filthy conditions found there. Miss Florence Nightingale, in a letter recently published, repeats these views, and enforces sanitary measures as our only safe-guard, stating that quarantine, isolation, and the like, by distracting the attention from such measures, may tend fatally to aggravate the disease, and she quotes Dr. Cunningham as authority.

All this must not be underestimated. The truth lies very probably in the particular cause of infection, but this seed must find a soil favorable for its growth and dissemination, and here we find abundant cause to enforce all sanitary measures, just as in the entire class of zymotic diseases.

As in consumption, we must have not only the bacillus tuberculosis, but must find conditions favorable for its development; an unhealthy mucous membrane lining the respiratory tract, its ciliated epithelium impaired, or destroyed, furnishing a soil fitted for its growth.

In the present lax condition of English surveillance of her commerce, it becomes our Government to exercise a doubly careful enforcement of our wisely framed quarantine laws, while it behooves every citizen to look especially after his own sanitary surroundings. In something of the same spirit which actuates the English government, a leading editorial

in the *Boston Medical and Surgical Journal* of Oct. 9, upon "Cholera and Rags," deprecates the action of our Government, and finds fault with the order issued by our indefatigable Surgeon-General Hamilton, forbidding the importation of rags for three months. The wisdom of such an order could only be called in question by the superficial or prejudiced critic.<sup>1</sup>

Having given so much space to the diseases in which bacilli are believed to play an important part, we must pass over more rapidly the group of diseases in which the round cell or micrococcal growths predominate. In this group have been classed, with greater or less evidences of a causative character, cholera of fowls, pyæmia and septicæmia in rabbits, swine-plague, pleuro-pneumonia of cattle, hydrophobia, small-pox, vaccine, gonorrhœa, whooping-cough, measles, scarlet fever, diphtheria and erysipelas.

The presence of micro-organisms is easily proven in the products of diphtheria. Ten years ago I demonstrated them in diphtheritic membrane. Recklinhausen, Klebs, Eberth, and many others have discovered them in many organs and tissues. Oertel and Eberth are very sure of the causal relations of the micrococcus diphtheria. Klebs produced diphtheria in animals by the inoculation of pure cultures. None are of greater value and interest than the studies of Drs. Wood and Formad. They inoculated pure cultures in a number of instances, resulting in the death of the animal. Micrococci were abundant in all cases. Last autumn I instituted a series of cultures from a portion of tracheal membrane removed after trach-

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<sup>1</sup>Space forbids any farther discussion of the cholera bacillus, but we would urge a careful study of Dr. Koch's address upon the cholera and its bacillus, delivered before the Imperial German Board of Health in Berlin, and translated and published in the *British Medical Journal*, August and September, 1884, at the close of which Prof. Virchow, after thanking Dr. Koch for giving this long and detailed account of his view, said: "I say decidedly for myself that, from the beginning, I thought it very probable that the bacillus was, indeed, the *ens morbi*; but from what I have heard to-day, my conceptions on the subject have arrived at a much greater degree of certainty."

eotomy. Careful microscopic examination was made at each inoculation, and the developing and the massing of the micrococci were carefully noted. Zoöglea masses were abundant in each instance. The tenth in the series covering a period of about 40 days was selected for inoculative experiments. From this six guinea-pigs were inoculated in the cornea of the eye. One died upon the second day, and three were killed on subsequent days. A membrane developed in the eye infected in all, and micrococci were numerous in each. The other two recovered with loss of the eye inoculated. During the inoculating experiments my assistant, Dr. Nelson, was infected and suffered a severe attack of diphtheria, from which he slowly recovered. Micrococci presenting the same appearance and characteristic massing were abundant in the proliferation about his tonsils. From this I reproduced in culture micrococci with the same characteristic appearance.

Fehleisen detected in several cases of erysipelas micrococci, especially in the parts and the periphery of the erysipelatous patch, at the very commencement of the process. He found them in the interstitial tissue, and also in the lymphatics, and in their neighborhood he found accumulation of leucocytes. He was able also to cultivate the organisms in a solid gelatine soil, and went on cultivating them to the twelfth and thirteenth generation. He noticed a different naked-eye appearance of the cultivated masses from that of cultivating masses of other septic micrococci. The cultivated organisms, when injected into a rabbit's ear produced, after an inoculation period of twelve to eighteen hours, typical erysipelas, spreading to the head and the neck. In the affected parts, the micrococci were again seen. Removing the rabbit's ears twelve hours after inoculation stopped the process. Bearing in mind some well-known observations by Nélaton, Thiersch, and Volkmann, that patients suffering from malignant

tumors improved, when contracting erysipelas, Fehleisen inoculated patients, some suffering from cancer of the breast, others from sarcomatous tumors, others from lupus, with the cultivated micrococci and produced, in seven out of nine inoculations, typical and in one case most severe erysipelas."

From the fluid in blisters of erysipelas patients I have cultivated and studied the micrococci very carefully. They were easily reproduced in a given series, but two or three injections and inoculative experiments failed of a development of the disease in the guinea-pig.

The relation of erysipelas to puerperal fever has long been suspected. An unfortunate series of cases occurring in the practice of a brother physician recently is worthy of notice. Three of the fatal cases I saw in consultation. Following a case of erysipelas early in January there supervened in his practice five fatal cases of puerperal fever, the last developed at about the tenth day, erysipelas following what seemed a slight abrasion in the middle line over the coccyx, up the back, and then diffusing laterally until it became general and before death had extended over quite the larger portion of the body. In bulbs infected at the bedside with secretion taken directly with much care from within the cervix uteri, micrococci were reproduced in rapid growth, and, in appearance, the micro-organisms could not be differentiated from the cultures from the blisters of erysipelas.

In the pus from gonorrhœa Neisser detected a micro-organism, a micrococcus; this he was able to cultivate and found its naked-eye appearances, as cultivated on gelatine, different from the septic micro-organism. Inoculations performed by him were not successful. Bockhardt has, however, recently repeated the experiment, cultivated the micrococci and obtained positive results or inoculations.

Dr. Queist, of Russia, reports that he has successfully cultivated vaccine virus, and that with this he has vaccinated with typical pustules and thereafter granting immunity against a second vaccination. No test has been offered as to the prevention of small-pox. He states that the micrococci developed into bacilli and these again into micrococci.

By the politeness of Dr. H. A. Martin, of Boston, we were enabled to inoculate bulbs directly from the animal serum. In these developed an abundance of micrococci single and in chains; they are very minute and active, combined in twos they resemble short bacilli and require high powers to differentiate. Our vaccine experiments, however, failed.

I would enter an earnest plea that every medical school should train a corps of competent observers, that each hospital set apart the needful appliances for the proper study of diseased tissues and secretions, and that the profession generally be requested to collect material which, in capillary tubes, enclosed in melted parafine, and other ways, may safely be transmitted by mail. By such means our present knowledge would be materially enhanced.

Although I have omitted much of real value, I believe we may conclude from this review that the time has passed when the critic of the germ-theory of disease can content himself with captious remarks "upon fashions in medicine, deluded followers of speculative theories, etc." As well might the geographer deny the existence of Africa because a topographical survey had not been made of its interior. All along the border lines of the unknown are enthusiastic explorers engaged in the difficult and dangerous work of investigation with a heroism and determined fortitude of a Livingstone or a Stanley. In these directions science is not without its martyrs. The investigations of a cholera commission in Egypt and India or yellow fever in Havana are not less danger-

ous than an expedition to discover the sources of the Nile or a ship's company in quest of the northwestern passage.

Let us, in common with grateful republican France, hold in loving remembrance her peasant-boy Pasteur and his school of followers ; with the great and learned empire of Germany recognize in Koch and his distinguished colaborers the important discoveries already made ; with England vie in doing honor to a Lister and his students who have revolutionized surgery ; and shall we forget in our own country a Sternberg, a Belfield, a Formad, and many others whose work has added to our national fame? We are glad to pay tribute of loving remembrance to Johns Hopkins, the founder of a University in whose halls we are now assembled, which ennobles science ; to a Senney who reaches a climax of national benevolence in founding a hospital ; and last, not least, to the railroad prince of America who enlarges the boundaries of science by his magnificent gift to one of New York's most famous schools of medicine. We emphasize the ingratitude of kings and emperors as we hold up to our sons the glowing picture of a republic. As scientists, however, we must remember that we lack political potency. For us, no " Harbor and River Bill," under the flattering representation of national commercial development, carries the open sesame of patronage and votes. A National Board of Health is shorn of its usefulness and unmeasured good through ostensible motives of economy, while our millions are expended with a lavish hand to aid " the power behind the throne." Just now, the personal aggrandizement of some possible President is, in political estimation, of far greater consequence and importance than the prevention of contagious and zymotic diseases which annually carry to untimely graves their hecatombs of victims.

Let the medical profession arise to its just prerog-

ative and power as conservator of the public health. Memorialize Congress to aid in the better solution of the important questions of preventive medicine, and the great wealthy government of the New, rival the Old World in a generous emulation in the settlement of questions fundamental to the health, happiness, and long life of her citizens.



